REMARKS

Claims 5-13, 16-18, 39-50, and new claims 51 and 52 remain in the application for further prosecution. Claims 1 and 38 have been canceled and replaced by new claims 51 and 52 to clarify the differences between the Applicant's device and the Shartle reference. Claims 5, 7, 13, 16, 39, 41, 47 and 48 have been amended to correct their dependency.

More particularly, the Applicant's device includes a capillary segment that defines a uniform volume of the sample liquid, which is positioned between two vents to atmosphere. In operation, the uniform volume is transferred from the segment through a separate transfer capillary that enters the segment between the two vents to atmosphere, while air enters the vents to replace the transferred liquid. The transfer capillary contains a hydrophilic or hydrophobic stop to prevent the uniform volume of sample from being transferred to the reagent well until desired.

Rejections Under 35 U.S.C. 102(b)

The Examiner has repeated his rejection for anticipation of Claims 1 and 38 by Shartle et al. ("Shartle"), referring in particular to Shartle's Fig. 5.

Claims 1 and 38 have been replaced. For Shartle to anticipate the replacement claims 51 and 52, he must describe each element of a claim, either literally or inherently. Shartle fails for 3 reasons.

1. His sample liquid is transferred by diluent from chamber 175 to mixing chamber 150 directly from one end of the sample-measuring capillaries (140 a and b), that is via stop 145. There is no separate transfer capillary entering 140 a/b between stops 145 and 146.

2. Stop-function 145 is not a vent to atmosphere but instead is intentionally blocked by 104/105 to assist in preventing premature flow of the sample into mixing chamber 150. This is a new feature in Shartle's invention, which is not found in the Applicant's device.

3. Since Shartle has no transfer capillary his device cannot have a capillary stop within the capillary.

In the following discussion, Shartle's devices of Fig. 1 and 5 will be shown to be inconsistent with the Applicant's device as claimed.

Comparing Fig. 1 and Fig. 5

The diluter shown by Shartle in Fig. 1 has most of the features of Fig. 5. The two diluters differ in the way in which excess sample liquid is handled. In Fig. 1, after measuring chamber 140 is filled excess sample will flow from flow directing chamber 130 into waste chamber 165. Then, when diluent is released from its chamber (175) it forces the measured sample (140) into mixing chamber 150. At the same time, diluent also flows into the waste chamber (148). It appears that a clean separation of diluent from the excess sample in the flow directing chamber 130 is not possible. This is described at column 16, beginning at line 38.

In contrast, Fig. 5 isolates the measured sample (140 a-b) from excess sample by closing valve 201/202, after which the measured sample is forced by the diluent into mixing chamber 150. The excess sample passes into the rupture chamber when valve 201/202 is closed, causing a pressure wave that breaches junction 147. In Fig 5, the diluent and excess sample would not be mixed so long as valve 201/202 remains closed.

A review of the operation in Fig. 5

Beginning at line 34 of column 13, Shartle describes the operation of the device shown in Fig. 5. In this design the liquid sample is divided in two parts by closing the valve (201/202). The part of the sample to be tested (140 a and b) is trapped between the closed valve (201/202) and the "stop-flow junctions" (146 and 145). It is pushed into mixing chamber 150 by rupturing the diluent chamber (175). The sample is transferred to mixing chamber 150 through junction 145 and not from a separate transfer passageway located between the 146 and 145 stop-flow junctions. The portion of the sample located between the junction of 140a and 140b and the valve 201/202 is blocked and therefore not pushed into mixing chamber 150 by diluent. Thus, in operation the device of Fig. 5 does not anticipate the claimed invention, nor could it be operated to perform the same function. For example, if valve 201/202 were left open, the diluent from 175 would exit into 150, 140 (aka 148), and 110. Clearly, closing valve 201/202 is essential in Shartle's Fig 5 device.

The Examiner is mistaken in suggesting that the transfer capillary is between rupture junction 147 and the intersection of 120 and 140a. When valve 201/202 closes, Shartle says that a pressure wave is created that ruptures junction 147, which causes excess liquid from 120 to flow into rupture chamber 148 (shown as 140 in Fig. 5), see column 13, lines 40-44. Therefore, even the excess liquid does not flow through the passageway dead-ended by valve 201/202. Consequently, neither the test sample nor the excess liquid is transferred through a capillary passageway located between two vents to the atmosphere.

It also should be noted that 145 in Fig. 5 is designated a stop-flow junction, but it is assisted by vent closing means 104/105. As Shartle explains at column 8, line 56 et. seq. the vent 101 is actually closed to permit air pressure build-up to assist stop-flow junction 145.

Therefore, in Fig. 5 the sample to be tested is not positioned between two vents to atmosphere, as the present claims require.

The Examiner has responded to the Applicant's previous arguments related to Shartle. The Applicant's comments follow:

- *"The sample wells [sic]110 of the Sharle [sic] is structurally capable of receiving a sample and there fore[sic] is a sample well for collecting a sample to be processed."* The Applicant's well is illustrated in several figures, most simply in Fig. 2. The well (R1) clearly is intended to hold a sample larger than the liquid to be tested, which is defined by the capillary between V1 and V2. Shartle merely refers to 110 as being a "sample application site", which appears not to be intended to hold liquid in excess of the sample to be tested.
- *"[T]he hydrophilic capillary passageway as seen in fig. 5, ref 120 is in communication with the sample well 110."* This comment is factually correct, but not relevant to Applicant's point, namely that 145 is not vented to atmosphere.
- *[S]ince the sample well is open to the atmosphere it can be a vent...The capillary passageway 120 and uniform volume segment 140a are located between vent 1 (110) and a second vent 104 that vents to the atmosphere...Therefore Shartle discloses a uniform volume between two vents to the atmosphere."* If the device on Fig. 5 is properly understood, when valve 201/202 is open all of the capillaries are filled with liquid. Therefore, if 110 is considered a vent, 147, 145, and 146 could also be considered vents. However, the liquid so contained is not a uniform sample to be measured. Alternatively, when valve 201/202 is closed, the uniform sample is defined as being within capillaries 140a and 140b (with some excess adjacent the valve). We have pointed out that when 104/105 is closed (according to Shartle to assist stop 145) then 145 should not be considered a vent to atmosphere.

Furthermore, it appears that stop 146 preferably is not vented to atmosphere (it is referred to as "internally vented"), since Shartle prefers to have no opening from which diluent could leak after 175 is ruptured (see column 17, lines 23-54).

- *"[T]he transfer capillary is the segment located between ref. 147...and the intersection of capillary 120 and 140 a...This is a capillary that exits the capillary of 120 and 140a and provides a sample to well 140".* The Examiner's understanding of the function of Shartle's Fig. 5 device is not correct. The measured sample is pushed by diluent from 175 into mixing chamber 150. There is no transfer capillary that empties 140 a and 140b from between vents to atmosphere into a chamber. This done when valve 201/202 is closed, which isolates 120 and the pressure wave ruptures 147, allowing excess sample to flow into 140 (actually 148, see column 13, lines 34-44). Therefore, the excess liquid is defined between closed valve 201/202 and 110, not between two vents to atmosphere.
- *"The Examiner points to the previous paragraph for the interpretation of the transfer capillary for Shartle. The capillary stop is seen in figure 5 as reference 147."* Regardless of whether there is a transfer capillary segment or not, as pointed out above, the capillary section entering at 147 only transfers excess liquid when valve 201/202 is closed. Therefore, a fixed volume of liquid is not transferred from between two vents to atmosphere.

The Applicants submit that in view of the differences discussed above, that Shartle does not anticipate the amended claims.

Rejection under 35 U.S.C. 103

Claims 1, 5-13, 16-18, and 38-50 have been rejected under 35 U.S.C. 103(a) as unpatentable (i.e. obvious) over McNeely, et al. (US 6,296,020)("McNeely '020") in view of

Kellogg, et al. (US 6,063,589("Kellogg") and further in view of McNeely, et al. (US 6,615,856)("McNeely '856").

The Examiner has repeated his previous rejections based on McNeely '020, Kellogg and McNeely '856. McNeely '020 does not show a sample well, which supplies a reagent well with a sample volume defined by a segment of a hydrophilic capillary defined by two vents. Instead, McNeely '020 has been cited for its teaching of physical principles, rather than for a device related to the Applicant's microfluidic device. Therefore, McNeely '020 is not a typical principal reference under 35 U.S.C. 103, which contains omissions to be supplied by the secondary reference.

In general, McNeely '020 shows devices for splitting liquid into multiple wells or combining several liquids in a single well, using passive stops. McNeely '020 evidently preferred using hydrophobic passageways with aqueous liquids, combined with hydrophilic stops (see column 3, lines 59-62, the discussion above and the claims). McNeely '020 does not show a sample well connected to a capillary passageway that contains a segment defining a sample volume, which is transferred to a reagent well. The Examiner's citations of the McNeely '020 patent were discussed in a table in the last amendment, to which reference may be made.

McNeely '020 fails to support the Examiner's position. McNeely '020 not only lacks the use of a hydrophilic capillary to transfer liquid, but he fails to describe a device that separates from a larger sample a defined volume in a capillary segment and transfers that defined volume to a reagent well. McNeely '020 appears to teach that use of a second liquid or a gas to force a first liquid past capillary stops. Also, since he appears to use hydrophobic passageways with water-based liquids, it is implied that capillary forces are not used to transport liquid.

Kellogg describes devices in which centrifugal force is used to transfer liquids after a sample liquid fills the group of capillaries used to define the sample volume to be tested. The sample volume is not defined by a portion of a hydrophilic capillary positioned between two vents, but instead an array of capillaries is defined as between a chamber at one end and the sample well at the other end (the excess sample having been sent using centrifugal force to the over flow well). Thus, Kellogg does not teach the use of a capillary segment that connects to a transfer capillary between two vents.

McNeely '020 does not show essential elements of the Applicants' claimed invention and forces liquid through with other liquids or gas. Kellogg relies on increasing centrifugal force to transfer liquid through his devices. There is no reason why one skilled in the art would consider a combination of McNeely '020 and Kellogg. The Kellogg devices are designed to move liquid and expel air with increasing centrifugal force and therefore are not combinable with the McNeely '020 devices. Kellogg would have to redesign his device to be operated by a driving liquid or gas as done by McNeely. Alternatively, McNeely '020 would have to be redesigned to operate by centrifugal force. Consequently, different devices would be provided, but not those of McNeely '020 or of Kellogg, since they have different objectives.

The McNeely '856 patent teaches a method of controlling fluid flow in a microfluidic device in which external valves and pumps are employed (see Abstract). Since capillary forces are not used by McNeely's devices, the flow of liquids is controlled by opening and closing vents. As he shows in Fig. 1 A-C, liquid flow is stopped beyond an air vent since the external force applied is not able to compress the air trapped in the dead-ended passageway. The general approach is discussed in the section entitled "Flow Barriers" (column 4, line 33 et seq.). As McNeely observes "if capillary forces cannot be relied upon, ...then alternative methods of

fluid control are needed" (column 4, lines 37-40). "An alternative to capillary stop junctions and the like are pneumatic pressure barriers" (column 4, lines 45-46). It appears then, that McNeely '856 is not pertinent to the Applicant's invention.

Consequently, the Examiner is asked to enter the proposed amendments and then to reconsider his rejection and allow the claims as amended. If further amendment is believed necessary, the Examiner is invited to contact the Applicants' attorney at the telephone number provided below.

Respectfully submitted,

4/9/08
Date

Harold N. Wells
Reg. No. 26,044
Kelley Drye & Warren LLP
333 West Wacker Drive, Suite 2600
Chicago, IL 60606
Attorney for Applicants
Telephone: (312) 857-2309